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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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AFFYMETRIX, INC
ATTN: CHIEF IP COUNSEL, LEGAL DEPT.
3380 CENTRAL EXPRESSWAY
SANTA CLARA, CA 95051

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)
	09/683,613	CHRISTIANS ET AL.
	Examiner	Art Unit
	Cynthia B. Wilder, Ph.D.	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed on June 2, 2004 is acknowledged and has been entered. Claims 1, 2, 6-11 have been amended. Claims 1-21 are pending. All of the amendments and arguments have been thoroughly reviewed but are deemed moot in view of the new grounds of rejection based on Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Objections and Rejections

3. The objections to the drawings are withdrawn in view of Applicant's amendment of the claims. The objection to the claims 7-11 as being improperly dependent is withdrawn in view of Applicant's amendment. The claim rejection under 35 USC 112 second paragraph as lacking proper antecedent basis is withdrawn in view of Applicant's amendment of claim 2. The prior art rejection under 35 USC 102(b) directed to claims 1-5, 9-15 and 19-21 is withdrawn in view of Applicant's amendment. The claim rejection under 35 USC 103(a) directed to claims 6-8 and 16-18 is withdrawn in view of Applicant's amendment.

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 1 is indefinite at the recitation of "using ribosome display" because applicant is relying on a technique of the prior art that has not been adequately describe or disclosed in the specification or claims and thus it cannot be clearly determined how the technique of ribosome display is utilized to tag the polypeptides. The specification and prior art teaches that ribosome display is based on *in vitro*-translation, in which both the mRNA and the protein product do not leave the ribosome. Therefore, it is unclear in the claimed method how ribosome display is involved in tagging polypeptides. For example, it unclear if the mRNA coupled to the protein product as in ribosome display is considered the tag for the protein product or not. Clarification is required as to how the technique of ribosome display is involved.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. It is noted that the preceding rejection is based on the Examiner's interpretation of the new claim limitation of "ribosome display". Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Kuimelis et al (WO 99/51773, October 14, 1999). Regarding claim 1, Kuimelis et al teach a method for screening polypeptides comprising: linking each of a plurality of polypeptides with a nucleic acid tag to obtained tagged polypeptides by ribosome display called ribosomal display particles and hybridizing the tagged polypeptides with an addressable capture probe array to immobilize

the tagged polypeptide on the array, wherein the probe array has at least one probe for each of the nucleic acid tag and screening the polypeptides on the solid support array (page 3, lines 4-8; page 5 to page 6, line 19; and col. 15, lines 3-6). Therefore, Kuimelis et al anticipates the claimed invention of claim 1.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuimelis et al (WO 99/51773, October 1999) and Gold et al (WO 93/0172, February 1993) in view of Fodor et al (US, 587,928, February 16, 1999). It is noted that the preceding rejection to claim 1 is based on a second interpretation of the new claim limitation ribosome display by the Examiner. Regarding claims 1-3, 6-13, and 16-21, Kuimelis et al teach a method for screening polypeptides comprising: providing a

plurality (population: page 6, line 15) of RNA-protein fusion complexes or ribosomal display particles as described by Gold et al., comprising a protein linked to its coding RNA (mRNA) and hybridizing the RNA-protein fusion complex or ribosomal display particles to an addressable array comprising a plurality of capture probe thus immobilizing the complexes or ribosomal display particles to the array, wherein the array has at least one probe for each of the complexes or ribosomal display particles and screening the polypeptides on the array (page 3, lines 4-8; page 5 to page 6, line 19; and col. 15, lines 1-6). Kuimelis et al teach that the array may include 10^2, more preferably 10^3, and most preferably 10^4 different RNA-protein fusion complexes attached to the probe array. Kuimelis et al teach the use of multiple hybridization tags having different sequences attached to RNA-protein complexes of the invention ((col. 6, lines 9-14). Kuimelis et al does not expressly teach wherein the different tags are attached to the mRNA of the ribosomal display particles.

Gold et al., as cited by Kuimelis et al., teach ribosomal display particles and there use in methods of screening or identifying target molecules. Gold et al. teach wherein the ribosomal display particles comprise mRNA covalently bound to polypeptide copolymers. Gold et al teach that the mRNA incorporated therein may include organic tags attached to the 5' end without difficulty and without harming the RNA for other functions. Gold state that thus each mRNA in the collection could have, for example biotin or any one of a number of small reagents affixed to the 5' end of the RNA. Gold et al state that alternatively, mononucleotides labeled with biotin could be used to initiate transcription. Gold et al state that the 5' end of the RNA would certainly not preclude translation by bacterial ribosomes, since those ribosomes are indifferent to the chemical nature of the 5' end as long as enough nucleotides are present upstream of the

initiating AUG and as long as those nucleotides contain appropriate sequence to cause initiation to occur (page 42, lines 8-27). Neither Kuimelis et al or Gold et al expressly teach wherein the DNA array as described by Kuimelis comprise a probe for each of the tags of the polypeptides nor do the references teach wherein the DNA array comprises at least 400 or 1000 or 10000 different oligonucleotide probes per cm^2.

Fodor et al teaches a method analyzing polynucleotide or a polypeptide sequence via hybridization to an oligonucleotide array. Fodor et al describe the array as a composition comprising a plurality of positionally distinguishable sequence specific reagents attached to a solid substrate, which reagents are capable of specifically binding to a predetermined subunit sequence of a preselected multi-subunit length (tag) (col. 2, lines 54-60). The reference teaches wherein the subunit may be a polynucleotide or a polypeptide (col. 2, lines 61-62). Fodor et al additionally teach wherein the oligonucleotide array may comprise from at least 50 oligonucleotides to an excess of one million oligonucleotides (col. 20, lines 5-23). Fodor et al teach that the method for analyzing polypeptides or polynucleotides using oligonucleotide probe arrays is useful because it provides a improved means for de novo sequencing of an unknown polymer sequence, for verification of know sequences and for mapping homologous segments with a sequence by reducing the number of manual manipulations required and automation of most of the steps. Fodor states that thus the speed, accuracy and reliability of these procedures are greatly enhanced (col. 2, lines 21-28). Therefore, in view of the foregoing one of ordinary skill in the art would have been motivated at the time of the claimed invention to have provided a an oligonucleotide array comprising at least 400 to 10000 oligonucleotides for the polypeptide screening method as taught by Kuimelis et al and Gold et al for the advantages taught by Fodor

et al. that by analyzing polypeptides or polynucleotides using oligonucleotide probe arrays, one provides a means of reducing the number of manual manipulations required and automation of most of the steps, therefore greatly enhancing the speed, accuracy and reliability of the these procedures (col. 2, lines 21-28).

Regarding claims 4, 5, 14 and 15, Kuimelis et al teach wherein the screening comprises determining the binding affinity of the polypeptides with a ligand, wherein said ligand is a drug candidate (Abstract and col. 5. lines 21-27 and col. 16, lines 12-13).

Claim Rejections - 35 USC § 103

10. Claims 12-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baskerville et al ((WO 99/54458, October 28, 1999) in view of Fodor et al (US, 587,928, February 16, 1999). Regarding claim 12, 13, 16-18, Baskerville teach a method for screening polypeptides comprising linking each of the polypeptides to nucleic acid tags to obtain tagged polypeptides; hybridizing the tagged polypeptide to a solid surface comprising probe (binding partner) sequences complementary to each of the nucleic acid tags linked to the polypeptides and screening the polypeptides for biological activity/function. Baskerville et al additionally teach that the solid surface may comprise of beads, chips or other planar surfaces, wells or columns. Baskerville et al teach that because there is no limit on the number of different possible nucleic acid tags, an essentially unlimited number of different (uniquely or specifically) tagged polypeptides can be produced and once produced, the tagged polypeptides can be analyzed via hybridization to DNA arrays (page. 23 line 21 to col. 24, line 15 and page. 26, line 4 to page 27, line 7; see also page 25, lines 16- 30 and Figure 3). The method of Baskerville et al differs from

the instant invention in that the reference does not teach wherein hybridization to the DNA array comprise a probe for each of the tags of the polypeptides nor does the reference teach wherein the DNA array comprises at least 400 or 1000 or 10000 different oligonucleotide probes per cm^2.

Fodor et al teaches a method analyzing polynucleotide or a polypeptide sequence via hybridization to an oligonucleotide array. Fodor et al describe the array as a composition comprising a plurality of positionally distinguishable sequence specific reagents attached to a solid substrate, which reagents are capable of specifically binding to a predetermined subunit sequence of a preselected multi-subunit length (col. 2, lines 54-60). The reference teaches wherein the subunit may be a polynucleotide or a polypeptide (col. 2, lines 61-62). Fodor et al additionally teach wherein the oligonucleotide array may comprise from at least 50 oligonucleotides to an excess of one million oligonucleotides (col. 20, lines 5-23). Fodor et al teach that the method for analyzing polypeptides or polynucleotides using oligonucleotide probe arrays is useful because it provides a improved means for de novo sequencing of an unknown polymer sequence, for verification of know sequences and for mapping homologous segments with a sequence by reducing the number of manual manipulations required and automation of most of the steps. Fodor states that thus the speed, accuracy and reliability of these procedures are greatly enhanced (col. 2, lines 21-28). Therefore, in view of the foregoing one of ordinary skill in the art would have been motivated at the time of the claimed invention to have provided a an oligonucleotide array comprising at least 400 to 10000 oligonucleotides for the polypeptide screening method as taught by Baskerville. One of ordinary skill in the art would have been motivated to do so for the advantages taught by Fodor et al. that by analyzing polypeptides or polynucleotides using oligonucleotide probe arrays, one provides a means of reducing the

number of manual manipulations required and automation of most of the steps, therefore greatly enhancing the speed, accuracy and reliability of the these procedures (col. 2, lines 21-28).

Regarding claim 14 and 15, Baskerville et al teach wherein the screening comprises determining the binding affinity of the immobilized polypeptides with a ligand wherein said ligand is a drug candidate (page 26, line 14 to page 27, line 7).

Regarding claim 19-21 Baskerville teach that an unlimited number of polypeptides may be tagged with a specific (different) nucleic acid (page 26, lines 4-6).

Conclusion

11. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Cynthia Wilder

CYNTHIA WILDER
PATENT EXAMINER
8/2/2004